I. Rejections under 35 U.S.C. §112, first paragraph

Claims 5-13 stand rejected under 35 U.S.C. §112, first paragraph, as the disclosure is allegedly enabling only for claims limited to nucleic acids which encode the protein of SEQ ID NO:2. Applicant respectfully traverses this rejection.

The rejection is moot with respect to canceled claim 8. Applicant has amended claim 5 to recite a polynucleotide encoding connective tissue growth factor (CTGF) polypeptide having characteristics as described, *e.g.*, molecular weight, biological activity. One of skill in the art could readily isolate a polynucleotide as claimed now that Applicant has more fully defined CTGF polypeptide. For example, the paragraph bridging pages 6 and 7 of the specification describes standard screening procedures which can be used to isolate a CTGF encoding polynucleotide. Consequently, Applicant believes that the amendment to the claim overcomes the rejection and respectfully requests that the rejection be withdrawn.

II. Rejections under 35 U.S.C. §112, second paragraph

Claims 5-13 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully traverses this rejection.

The rejection is moot with respect to canceled claim 8. Claim 5 is allegedly indefinite as to "functional fragment thereof". Applicant has amended claim 5 to delete this language solely for the purpose of advancing prosecution and such amendment should not be taken as an admission against Applicant's interest with respect to the invention described in the specification.

Claim 8 is indefinite as to the recitation of degeneration sequences. Again, Applicant has canceled claim 8 solely for the purpose of advancing prosecution.

Claim 9 is allegedly indefinite for the use of "vectors" and claims 10 and 11 are indefinite because claim 9 lacks antecedent basis for "the vector" and "a DNA vector". Claim 9 has been amended to recite "a vector", thus providing antecedent basis for claim 10. Claim 11 has been amended to delete the term "DNA" from the phrase "a vector".

In light of the amendments to claims 5 and 9 and the cancellation of claim 8, Applicant respectfully requests that the rejections under 35 U.S.C.§112, second paragraph be withdrawn.

III. Rejections Over the Prior Art

Claims 5-12 stand rejected under 35 U.S.C.§102(a) as allegedly anticipated by Ryseck, et al. Applicant respectfully traverses this rejection.

Applicant has provided a declaration under 37 CFR §1.131 by Dr. Gary Grotendorst, one of the two inventors of the present invention, which overcomes the Ryseck reference. Specifically, the declaration states that the clone and sequence of CTGF were obtained in Dr. Grotendorst's laboratory in the United States and submitted to GenBank on July 17, 1990, prior to the May 1991 publication date of Rysek. The Office Action states that a comparison of the amino acid sequence of fisp-12 and CTGF reveals only 13 discrepancies in the region between 86 to 392. The Office Action states that there is greater divergence in the region preceding residue 86. The Office Action states that Ryseck identifies this region as a signal sequence which would not affect protein activity.

It is well known in the art that a typical signal sequence is about 15-25 amino acids in length. In fact, on page 227 of Ryseck, line 5, the authors state that the signal sequence of fisp-12 is only 21 amino acids (also see FIGURE 3). The cleavage site for the signal sequence is between residues 25 and 26 (page 226, column 2, second paragraph). Therefore, the sequence divergence found in amino acids 26-86 is significant and therefore the fisp-12 protein described by Ryseck is distinguishable from CTGF of the present invention.

Further, prior to the May, 1991 date of the Ryseck reference, Dr. Grotendorst had immunoaffinity purified CTGF and shown that it had mitogenic activity in a DNA synthesis assay using NRK fibroblasts. EXHIBIT A shows laboratory notebook pages from Dr. Grotendorst's lab for experiments which were performed prior to the date of the Ryseck reference showing that immunoaffinity purified CTGF has mitogenic activity.

The identification of PDGF-like activity in HUVE cell conditioned media prompted the cloning and the isolation of a full length CTGF clone from a HUVE cell library (see

Examples of the present patent application). The clone, designated DB60, was isolated from a HUVE cell cDNA library in λgt11 screened with anti-PDGF antibody.

The clone encoding the entire open reading frame of the CTGF protein was isolated prior to the May, 1991 date of the Ryseck reference.

Consequently, Ryseck is not available as a reference and Applicant respectfully requests that this rejection be withdrawn.

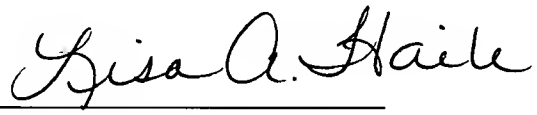
Claim 13 stands rejected under 35 U.S.C.§103 as allegedly unpatentable over Ryseck, et al. While Applicant respectfully traverses this rejection, Applicant submits that in light of the declaration under 37 CFR §1.131 by Dr. Grotendorst (discussed above), Ryseck is not available as a reference. Applicant respectfully requests that this rejection be withdrawn.

In summary, for the reasons set forth herein, Applicant maintains that claims 5, 9-13 and 29-30 clearly and patentably define the invention and respectfully requests that the Examiner reconsider the various grounds set forth in the Office Action. Applicant requests entry of the claims as amended on the grounds that they are in better form for consideration on appeal. In the alternative, Applicant submits that this case is now in condition for allowance, and therefore respectfully requests reconsideration and reexamination of the present application, and allowance of the case at an early date.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative would welcome the opportunity. Applicant's representative can be reached at (619) 678-5070.

Respectfully submitted,

Dated: February 12, 1996



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